The REDUCED Trial: REDucing the Utilization of CEsarean sections for Dystocia

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TABLE OF REVISIONS

Version	Date of revision	Comments
1	May 31, 2017	- Original protocol
2	Sept 8, 2018	- Clarified that our study population includes primiparous women "at term (≥37 weeks), with a vertex presenting singleton fetus" - Provided an updated definition for neonatal asphyxia - Updated this paragraph of the statistical analysis: "The intervention period for the study will be taken as starting with the first day of roll-out (initiation complete at that site) of the guidelines until the completion of the program at all sites, with baseline and post-intervention encompassing the two year and four year periods before and after. The primary analysis will be performed on data for the period of time from completion of all site initiation (December 1 2017, until a 2 year period has expired from the initiation of the final intervention site (November 30th 2019). A subsequent 4 year analysis is also planned for data up to November 30th 2021. Occurrence of CS will be assessed over baseline and post-intervention using a repeated mixed effects logistic regression model following a constrained baseline approach which confines group differences to the post-intervention period, assuming no systematic difference during the baseline period. The random effects will include site and period within site. Having fewer than 40 sites, a small sample correction will be applied to the standard error for group differences underlying significance tests and confidence interval construction. As a secondary analysis, we will include data from the intervention period reflecting the site-specific dates for completion of the intervention (1st site completed initiation Feb 1 2017), incorporating a linear time trend to accommodate the potential for confounding of an underlying secular trend."
3	April 25, 2019	- Added labour culture survey methodology. - Added three secondary outcomes, including: postpartum uterine artery/pelvic artery embolization; postpartum hysterectomy; and postpartum maternal intensive care unit (ICU) admission. - Added this statement to the statistical analysis: "The model will include year and treatment plus treatment by year interaction over the intervention period, with corresponding random effects by site".
4	August 12, 2019	- Added the 2014 ACOG/SMFM guidelines. - Added methodology regarding chart review to determine the percentage of cesarean sections for dystocia that were done following the ACOG/SMFM guidelines
5	February 3, 2020	- Changed the dates for the chart review from a one-year period from Dec 1, 2018 to Nov 30, 2019, to a two-year period from Dec 1, 2017 to Nov 30, 2019. - Updated the statistical analysis section: "The primary analysis will include individual level data from all sites from the baseline period (2015 to 2016) and follow-up thereafter in both arms. The intervention period will defined separately for each intervention site according to the date of completion of implementation of the program (which

Version	Date of revision	Comments
		varied for the 13 intervention sites from January 31, 2017 to November 30, 2017). Data from the implementation phase (nominally one to two months) will be excluded as a wash-out period. The first intervention period ends November 30, 2019 (two years after completion of site initiation at all intervention sites), and the second intervention period will end November 30, 2021 (four years after completion of site initiation). CS rates will be assessed using repeated measures mixed effects logistic regression applied to individual births. We will apply a constrained baseline approach to adjust for pre-intervention data. Explanatory variables (fixed effects) in the model will include time period (in 6 month intervals), and indicators for intervention and post-intervention phases in the intervention sites. The post-intervention parameter will represent the primary measure of efficacy. Corresponding site-specific random effects will be included for all fixed effects". - Note that the statistical analysis section was updated <u>prior</u> to the study team receiving the final data for the trial.
6	April 27, 2020	- As a result of the COVID-19 pandemic, the REDUCED Trial was ended on Feb 29, 2020 (i.e. prior to the WHO declaring COVID-19 as a global pandemic on March 11, 2020), instead of Phase 1 being ended on Nov 30, 2019 and Phase 2 being ended on Nov 30, 2021. See Appendix 1. - Note that this change was made <u>prior</u> to the study team receiving the final data for the trial. - Changes in dates in the protocol are bolded.

The REDUCED Trial: REDucing the Utilization of CEsarean sections for Dystocia

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Summary

This project is a clustered randomized controlled trial of a knowledge translation intervention of new guidelines for the diagnosis of poor progress in labor. The intent is to reduce the rate of cesarean section (CS) in first time mothers without increasing maternal or neonatal morbidity.

Background: Cesarean section (CS) rates are increasing dramatically in Canada and rest of the western world. Preventing CS in first time mothers is the most effective way to eventually reduce the overall CS rate. The most common reason for CS in labor is dystocia or poor progress in labor. Poor progress in labor has been diagnosed for the last 60 years when the rate of cervical dilation deviates from the ideal rate described by the "Friedman's curve". Recent studies in contemporary populations have suggested that labor in many women does not progress as fast as expected by this curve, and yet can still result in natural delivery. One of the key findings is that it appears that the active phase of labor may be delayed in many subjects until 6 cm of dilation is achieved. This is a significantly delayed onset to the active phase of labor compared to what physicians currently expect. These recent studies have formed the basis of new American clinical practice guidelines for monitoring the progress of labor and for diagnosing poor progress of labor (similar updated labor guidelines have not been adopted in other countries, including Canada). It is hoped that uptake of these new guidelines will substantially reduce the rate of CS in labor. Unfortunately, there is evidence that guidelines alone are unlikely to bring about practice change. However, tailored implementation strategies targeting relevant physician and nursing barriers and leveraging existing facilitators can be highly effective in increasing the uptake and use of new guidelines into practice.

Primary Study Question: Does the implementation of an evidence-based, theory-driven knowledge translation strategy to apply new labor progress guidelines, result in a reduction in the risk of cesarean section in labor for first time mothers, at term (≥37 weeks), with a vertex presenting singleton fetus?

Study Design: Clustered randomized controlled trial (RCT) of Alberta hospitals.

Methods: This is a clustered-RCT using a cross forward design. Based on preliminary analysis of Alberta data we have a sufficient number of participating centres to detect a 25% reduction in the risk of CS. The intervention will be designed as an evidence-based, theory-driven program to bring about provider-level behavior change. Physician and nurse barriers and facilitators will be explored using a theory-structured survey. Findings will be mapped to the Capability-Opportunity-Motivation-Behavior Framework (COM-B) and Behavior Change Wheel generating candidate intervention functions. These will guide the literature based identification of appropriate candidate interventions. Candidate strategies will then be assessed using APRAISE (Affordability, Practicability, Effectiveness/Cost Effectiveness, Acceptability, Safety and Equity) and then finalized for physicians and nurses, respectively. We will use a labor culture survey to assess differences in unit culture between intervention sites and to see if those differences may explain any variation in uptake of the recent guidelines.

Study Team: The study team includes experts in clinical trials, knowledge translation, intrapartum care, nursing education, neonatology, and health economics. It also includes representatives from two key end user groups, the Alberta Perinatal Health Program and the Alberta Health Services Maternal, Neonatal, Child and Youth Strategic Clinical Network who are providing substantial in kind support.

Background

New American clinical practice guidelines for monitoring the progress of labor[1,2] have been developed based on recent studies in contemporary populations[3,4]. If integrated into routine clinical practice, they may reduce the number of women diagnosed with dystocia (poor progress of labor) and therefore reduce the rate of cesarean section. There is strong evidence that guidelines alone are unlikely to bring about practice change and require a formal implementation strategy[5], tailored to address provider barriers, facilitators and context to engineer sustained evidence use. The ultimate goal of the REDUCED Trial is to reduce the number of cesarean sections performed in first time mothers. To achieve this goal, we will use an evidence and theory driven intervention to optimize guideline use by labor and delivery providers in a multi-center cluster randomized controlled trial. We will assess the effectiveness, quality and context of the guideline use and the impact on cesarean section rates, while rigorously monitoring for potential harms using high fidelity data. While reducing the CS rate is a highly desirable patient, provider and systems-level outcome, achieving reductions in the CS rate has proven challenging[6]. This project is creative and likely to succeed in reducing cesarean section rates as it is based on translating a relatively simple guideline to intrapartum care providers, using audit/feedback methods to monitor individual and site level uptake of guidelines and proactively addressing barriers to implementation. We are confident that this novel approach carried out by our experienced and well qualified team can reduce CS rates in Alberta while providing a template for similar initiatives across Canada.

Cesarean section (CS) rates have increased steadily in Canada and the Western world for the past 60 years. Approximately 28% of Canadian women deliver by CS. The rate of repeat CS dropped in the 1980's due an increase in vaginal birth after cesarean section (VBAC). However, this trend is reversing as women increasingly opt for a planned elective repeat CS[7]. This underscores the importance of preventing the first CS in order to lower the overall rate. The most common cause of the first CS is dystocia or poor progress in labor[8]. The standard method for diagnosing dystocia is to compare the patient's rate of cervical dilation in labor with the expected rate on the Friedman curve. However, Friedman's data came from observing only 100 primiparous women in labor only one of whom had a CS[9]. The usefulness of the Friedman curve was never confirmed with clinical trials, but it was rapidly and widely adopted. In most labor and delivery units, a patient's cervical dilation is displayed on a partogram which includes clear indicators of poor progress and at what point "action", augmentation or CS, should be considered. Recently, labor progress was examined in a contemporary population in a large NIH funded multi-centre study. The Consortium for Safe Labor group described the rate of cervical dilation in 62,415 women who had vaginal deliveries and did not experience any maternal or neonatal complication[4]. This data suggests that in many women, spontaneous vaginal delivery occurs despite much slower rates of cervical dilation than those expected by the Friedman curve. A key finding is that the active phase of labor may be delayed until after 6cm of dilation is achieved. This is clinically meaningful as the expectation of current intrapartum care providers is that the active phase begins at 3-4cm. It is recommended that CS for dystocia not be performed in latent labor as poor progress in this phase is difficult to judge. However, based on the Consortium for Safe Labor data, many women are not in the active phase until 6cm dilation. Therefore, many women are being incorrectly diagnosed with dystocia in what is still their latent phase and having an unnecessary CS. The Consortium for Safe Labor study and similar data from a large sample of women undergoing induction of labor have been strongly endorsed by US experts and have formed the basis of new American clinical practice guidelines[1,2]. The new guidelines for the diagnosis of dystocia clearly offer the opportunity to reduce CS rates. However, calls for immediate widespread adoption without testing should be tempered by the fact that the impact of implementing these guidelines on maternal and neonatal outcomes is largely unknown. An unavoidable effect of implementing these guidelines is that fetuses will be exposed to more time in labor and therefore potentially increased risk. It is important to note that the Consortium for Safe Labor data were based only on women who eventually delivered vaginally without any maternal or neonatal complication. Therefore, **it is imperative that the effect of these guidelines on CS rates, other maternal outcomes and neonatal outcomes be assessed in the most rigorous study design possible, a randomized controlled trial.** Furthermore, if successful in reducing the CS rate, the REDUCED trial will be a substantial catalyst for the widespread adoption of this new approach to labor management.

Study Design: Cluster randomized controlled trial of a knowledge translation intervention of new guidelines for the diagnosis of poor progress in labor. The intervention will be randomized to centres (the clusters) in Alberta that provide intrapartum care, have facilities to perform cesarean section and deliver at least 70 primiparous women annually, with stratification based on facility type and geographic location. Clustering by centre and not individual caregivers (nurses/physicians) is necessary to prevent leakage or crossover of the intervention to controls. As all participating centres will eventually receive the intervention, the biostatistician will generate a randomization into two "waves". The intervention will be introduced sequentially by strata (Calgary, Edmonton, regional centres, rural centres) to the first "wave" hospitals in multi-week run-in periods after which those strata will be revisited for roll-out to the second "wave" hospitals.

Primary Study question:
Does an evidence-based, theory-driven Knowledge Translation intervention aimed at increasing the use of new clinical practice guidelines on labor progress change the rate of cesarean section (CS) in labor for first time mothers without increasing maternal or neonatal morbidity?

Primary Outcome: Cesarean section in labor for primiparous women at term (≥37 weeks) with a singleton vertex presenting fetus.

Secondary outcomes: Adverse neonatal and maternal outcomes including:

Neonatal:
a) Perinatal death;
b) Neonatal Asphyxia: intrapartum stillbirth or neonatal death from asphyxia (Perinatal Society of Australia and New Zealand coding)[10] or Neonatal Intensive Care Unit admission and at least two of: a. Apgar score of ≤5 at 10 minutes; b. Mechanical ventilation or chest compressions for resuscitation within 10 minutes; c. Cord pH < 7.00 (venous or arterial), or arterial base excess ≥ 12 at birth;
c) moderate or severe asphyxia or meets criteria for therapeutic cooling; and
d) sepsis or suspected sepsis.

Maternal:
a) post partum hemorrhage;
b) blood transfusion;
c) postpartum uterine artery/pelvic artery embolization;
d) postpartum hysterectomy; and
e) postpartum maternal intensive care unit (ICU) admission.

Other secondary outcomes: overall CS rate in primiparous women, overall cesarean section rate, rate of successful trial of labor, induction rate, augmentation of labor rate, duration of labor, and cervical dilation prior to cesarean section.

Implementation outcomes: Implementation quality (80% provider education completion pre-trial), site responsiveness (attendance and website tool access rates, attendance at feedback sessions by profession, frequency of coaching access), guideline adherence (adherence rate by site), and adaptation (implementation toolkit element use by site). Qualitative process and summative outcomes will capture how and why implementation was executed, by site, explore intrapartum and site leader perceptions of implementation, gather feedback on the implementation toolkit elements and utility.

Randomization.
A computer generated random allocation sequence will be created by the study statistician. Randomization will be stratified by type of site: urban or community.

Evidence-Based, Theory-Driven Intervention Design
The intervention itself is comprised of two parts: the clinical practice guidelines and the implementation strategy[11] which was designed using an integrated KT strategy[12] involving

collaborative efforts of the research team, intrapartum providers and leaders . The evidence base of the intervention is the data from the Consortium for Safe Labor study[4] and Harper et al[3]. The findings were operationalized in the American College of Obstetricians and Gynecologists (ACOG)/Society for Maternal Fetal Medicine (SMFM) guidelines[1,2]. The 2012 guidelines[2] provide definitions for arrest disorders in labor:
1. Failed induction of labor: Failure to generate regular (e.g. every 3 minutes) contractions and cervical change after at least 24 hours of oxytocin administration, with artificial membrane rupture if feasible.
2. First stage arrest: >=6cm dilation with membrane rupture and no cervical change for >=4 hours of adequate contractions or >=6 hours if contractions are inadequate.
3. Second stage arrest: No progress (descent or rotation) for >=4 hours in nulliparous women with an epidural or >=3 hours in nulliparous women without an epidural.

The 2014 ACOG/SMFM guidelines[1] provided additional guidance for the diagnosis of arrest disorders in labor for nulliparous women, which was also shared with the intervention sites:

First stage arrest
- A prolonged latent phase (e.g., >20 h in nulliparous women) should not be indication for cesarean delivery.
- Slow but progressive labor in first stage of labor should not be indication for cesarean delivery.

Second stage arrest
- A specific absolute maximum length of time spent in second stage of labor beyond which all women should undergo operative delivery has not been identified.
- Before diagnosing arrest of labor in second stage, if maternal and fetal conditions permit, allow at least 3 h of pushing in nulliparous women. Longer durations may be appropriate on individualized basis (e.g., with use of epidural analgesia or with fetal malposition) as long as progress is being documented.

Pre-Implementation Phase:
Implementation will be guided by the Knowledge to Action Framework[13] intervening at the level of care providers and the site. Pre-trial work is currently underway to assess guideline adaptability and implementability (ADAPTE II and GLIA 2.0 tools) by recruiting of a small cadre of providers. Site-based audits will establish the nature and magnitude of the practice gap, increase understanding of current state and enable early engagement at the site/provider level. Current CS rates and frequency of CS in labor at ≤6cm of dilation data for the study centres show that since the publication of the Consortium for Safe Labor data in 2012 there has been no observable changes in CS rates and the frequency of CS at ≤6cm in Alberta. Therefore, we think it is unlikely that this data or the new guidelines are influencing practice and a significant practice gap remains. Two theory-driven steps[14-16] will be used to elicit barriers/facilitators and change readiness using focus groups and online surveys in care providers and site leaders, respectively[17] A theoretical framework of behavior change domains will structure focus groups and survey questions[14]. Findings from these assessments will be mapped to behavior domains that are linked to an intervention design framework (Capability-Opportunity-Motivation-Behaviour)[16]. Relating domains to interventions in this way will generate a set of candidate interventions on the Behaviour Change Wheel that can be assessed for goodness of fit for the trial context, feasibility, risks and cost[18]. Context assessment using the Consolidated Framework for Implementation Research[19] will be used to systematically assess the individual, intervention, organizational and contextual-level facets of implementation[20]. A reliable readiness assessment tool will be used to understand current change readiness prior to trial kick off[21,22]. This process will allow us to develop interventions that will act on provider and site-based organizational barriers and facilitators, readiness and contextual factors, supplemented with access to KT/Implementation coaches, and an asynchronous web-based implementation toolkit.

Implementation Phase:
Interactive guideline dissemination will occur at provider-led kick off meetings, in partnership with administrative and clinical leaders. Meetings will be held with physicians and nurses to optimize engagement and interactivity. Several obstetrical medical and nursing volunteers have already

self-identified as potential clinical champions for the proposed trial. Based on our interactions with intervention site providers and leaders, we believe there is currently low general awareness of new guidelines, moderate readiness for change, and moderate-high tension for change. Key messages such as "avoid CS before 6cm for dystocia" etc. will be used to capture the essence of the guidelines for ease of use. Other specific strategies may include a large visual labor progress graph with a curve based on the Consortium for Safe Labor data displayed in all labor and delivery rooms. Educational supports will be developed to support and enhance in-person learning. Personalized login information will be provided to all physicians and nurses starting at the implementation kick-off meeting. Implementation will be facilitated by trained KT Advisors who will support site champions. . Implementation quality will be estimated by ensuring 80% of site providers have attended/completed the education units prior to trial commencement, and by ongoing KT Advisor assessment reports of intervention adherence, adaptation, and site responsiveness[23].

Post-Implementation Phase:
Site-based audit feedback will be provided every 3-6 months to monitor uptake, and to improve post-trial sustainability. Audit-feedback forms will be modeled on pre-existing Alberta Health Services dashboards that are familiar to providers. Qualitative interviews will be undertaken as part of a process evaluation to understand how and why guidelines and elements of the implementation toolkit are (or are not) being used, assess tool utility, sustainability and to explore provider/site leader perspectives on implementation. Factors have been designed into the implementation process to hedge ongoing sustainability of both the intervention and the outcomes[24-26]. Audit-feedback and clinical championship will transition as a standing item that can be revisited using pre-existing organizational quality infrastructure. The web portal and educational resources will be transitioned to the APHP. A strong pre-existing data sharing partnership with APHP will facilitate ongoing site audit data infrastructure. As the trial nears completion, the nature and strength of findings (outcomes and cost data) will be used to advocate for additional operationally-funded implementation resources to facilitate scale and spread at remaining sites.

Sample Size/Feasibility
Our sample size calculation is based on the assumption that a 25% relative risk reduction can be achieved with the intervention, i.e. a drop from 32% to 24%. Based on APHP data from 2009 to 2014, we have estimated the intra-cluster correlation (after adjustment for prior 5 year rate) as .002, but to be conservative we have assumed an ICC of .01 (well above the upper 95% confidence limit). Using the conventional adjustment for clusters, yields a requirement for 26 centres to provide at least 80% power at the usual (two-sided) 5% significance level. Simulations based on the observed 2014 instances of primipara birth in the 26 participating hospitals show that we have power exceeding 80% to detect even a 10% relative risk reduction.

Data Collection
The Alberta Perinatal Health Program (APHP) collects perinatal data from the provincial delivery record for all hospital births in Alberta. Data from the delivery records is validated through detailed computer programming that double checks all variables. All the stillbirths or neonatal deaths are captured by APHP.

APHP data is validated with Alberta Vital Statistics data for all deaths. Data is available for a number of variables ie: maternal demographics, type of labor, duration of labor, route of delivery, cervical dilation prior to CS, Apgars, neonatal resuscitation, cord blood gasses, post partum hemorrhage, maternal transfusion, and neonatal admission to NICU. Information is available for individual sites and practitioners. To assess neonatal outcomes such as asphyxia, data will be obtained from the Edmonton and Calgary site data of the Canadian Neonatal Network (CNN). Neonatal outcomes will include: intrapartum stillbirth, neonatal death, 5 minute Apgar score<7, cord pH<7.0 with base excess <12 mmol/l, moderate or severe asphyxia (Sarnat criteria) and therapeutic cooling. The evaluation of the neonatal outcomes will in collaboration with an emerging surveillance program which is monitoring the rate of neonatal asphyxia in Alberta. The data abstractors for the APHP and CNN will not be involved in the trial and will be unaware of site allocation. The data will be provided as in-kind support by the APHP. Given that data on at least 22,000 subjects will be provided this is an in-kind support equivalent to approximately 4 million dollars.

We will use a previously validated labor culture survey to assess differences in unit culture between sites and to see if these differences may explain the variable uptake of the guidelines. The labor culture survey has six subscales that include the following: best practices to reduce cesarean delivery, cesarean safety, fear of vaginal birth, maternal agency, physician oversight and unit microculture.[27] The survey will also include questions related to participant and unit engagement with the REDUCED guidelines.

The labor culture survey will be an online survey, which will be emailed to physicians and nursing staff at intervention sites in fall 2019. The survey will be administered by Research Electronic Data Capture (REDCap), which is a secure, browser-based application designed to support electronic data capture. The Clinical Research Unit (CRU) in the Faculty of Medicine at the University of Calgary is the REDCap host.

[April 27, 2020 update: Due to possible effects of the COVID-19 pandemic on the trial, an urgent steering committee meeting was convened on April 24, 2020. The decision was made to terminate the study as of February 29, 2020 (i.e., prior to the World Health Organization [WHO] declaring COVID-19 a global pandemic on March 11, 2020), instead of Phase I ending on November 30, 2019 and Phase 2 ending on November 30, 2021. This decision was made prior to the study team receiving the final data for the trial. The official statement of the steering committee regarding the end of the REDUCED Trial due to the pandemic can be found in Appendix 1. The dates in this version of the protocol reflect the new end date of the trial of February 29, 2020, and changes are bolded].

Data collection will include retrospective (baseline) data for the two years prior to the roll out of the intervention (2015 and 2016) and will continue until 27 months after the completion of implementation for all sites (**February 29, 2020).** Intervention and post-intervention periods will be defined for intervention sites according to their dates of initiation and completion of implementation.

A random sample of obstetrical charts will be reviewed from the 13 intervention sites during the **27 month** period from Dec 1, 2017 to **February 29, 2020** to determine the percentage of cesarean sections for dystocia that were done following the ACOG/SMFM guidelines. A minimum of 50 charts per site will be reviewed. If there are fewer than 50 cesarean sections for dystocia at a given site, then all of the dystocia cases during the two-year period will be reviewed.

Statistical Analysis

The analysis will be conducted independently by the study statistician (RB). The primary outcome will not be changed during analysis. The trial with an explicit statement of the primary outcome will be registered at clinicaltrials.gov.

The primary analysis will include individual level data from all sites from the baseline period (2015 to 2016) and follow-up thereafter in both arms. The intervention period will defined separately for each intervention site according to the date of completion of implementation of the program (which varied for the 13 intervention sites from January 31, 2017 to November 30, 2017). Data from the implementation phase (nominally one to two months) will be excluded as a wash-out period. The intervention period ends February 29, 2020 (27 months after completion of site initiation at all intervention sites).

CS rates will be assessed using repeated measures mixed effects logistic regression applied to individual births. We will apply a constrained baseline approach to adjust for pre-intervention data[28]. Explanatory variables (fixed effects) in the model will include time period (in 6 month intervals), and indicators for intervention and post-intervention phases in the intervention sites. The post-intervention parameter will represent the primary measure of efficacy. Corresponding site-specific random effects will be included for all fixed effects[29].

Having fewer than 40 sites, a small sample correction will be applied to the standard error for group differences underlying significance tests and confidence interval construction[30].

If the study has null results it will be important to try and determine if this were due to the ineffectiveness of the guidelines or poor adherence. Therefore, we also plan to assess indicators of guideline uptake such as changes in: duration of labor, time from admission until CS in non-progressing labors and rates of CS for dystocia <6cm.

Descriptive statistics will be used to characterize the labor culture at each site. We will use multiple linear regression to assess the relation between post-intervention percent change in cesarean section rate and site-level sub-scale means in the labor culture survey. In addition, we will examine the association between change in cesarean section rate and adherence to the guidelines for each site by simple linear regression.

Economic analysis
An economic evaluation will be conducted alongside the trial. The time horizon for the analysis will be to hospital discharge for both mother and baby. Costing will include the cost of the knowledge translation intervention implementation of the intervention including staff hours for participants and trainers, production of print materials, audit and feedback and also health care utilization during labor and delivery (CS rates, labor time, length of stay for mom and baby). The resource utilization, and costs, for costing the KT intervention will be collected by study team alongside the trial. Data on health care resource utilization, and the associated costs, will be collected as part of the trial from APHP and the Discharge Abstract Database of the Canadian Institute of Health Information. Outcomes will include maternal and neonatal morbidity/mortality, and patient experience also collected from administrative data.

Sources of Bias
We anticipate that some reviewers would prefer a broader intervention aimed at multiple risk factors for CS. However, existing clinical trial data does not suggest that reducing exposure to commonly touted risk factors for CS such as labor induction, epidural anesthesia or continuous fetal heart rate monitoring are effective at preventing CS[6,31,32]. Furthermore, a recent multi-centre clustered RCT in Quebec evaluated a comprehensive multi-modal program and were only able to reduce CS rates by 1.8%[33]. Other complex strategies such as the active management of labor have also been ineffective at clearly reducing CS rates [34,35]. We also anticipate that the simplicity of our intervention will improve adoption as increased complexity of an innovation has been shown to inhibit its adoption[32]. The main source of bias in our study is contamination or crossover of the intervention to control sites which could make it difficult to demonstrate a change in the primary outcome. While possible we think this is unlikely as the vast majority of physicians providing maternity care in Alberta work at only one hospital and we do not anticipate large numbers will change hospitals over the course of the trial. None the less crossover is a real concern. However, our data will allow us to at least monitor if unexpected changes occur at control sites. Another possible source of bias is that practitioners will be insufficiently incentivized to change. Judging from the strong support we have seen so far from provider representatives we think this is unlikely. Furthermore, we will provide specific and meaningful incentives for providers such as reimbursement for time and continuing education credits.

Data Safety Monitoring Committee (DMSC)
Data will be provided by APHP. The members will be Tracee Pratt (Executive Director, Royal Alexandra Hospital), Dr. Reg Sauve (University of Calgary) and Dr. Bill Fraser (Director of the Research Centre of the CHUS hospital). These individuals have extensive knowledge of the subject and experience in clinical trials. The safety analysis will be performed for data up to June 30, 2018 as this is the midway point to the primary analysis.

Timeline
This project will be completed within 3 years. Transitioning control sites to intervention sites will begin **following the COVID-19 pandemic, if Phase 1 of the trial is considered successful.**

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APPENDIX 1

REDUCED TRIAL STEERING COMMITTEE'S STATEMENT REGARDING THE END OF THE REDUCED TRIAL DUE TO COVID-19 PANDEMIC

(April 24, 2020)

Given the impact of the COVID-19 pandemic, data collection for the REDUCED Trial will be considered ended on February 29, 2020 (i.e., prior to the World Health Organization [WHO] declaring COVID-19 a global pandemic on March 11, 2020), instead of Phase 1 ending on November 30, 2019 and Phase 2 ending on November 30, 2021.

Labour management post-pandemic has materially changed our ability to move forward with our research for a number of reasons. Currently, the physicians' and nursing staff's focus is on COVID-related issues, and we anticipate that caregivers and their patients will be less patient during labour. Furthermore, there are documents, such as the Calgary Zone Women's Health's *Patient Screening and Fever Management During COVID-19*[36], which includes guidance that is not congruent with the REDUCED guidelines (e.g., avoiding delayed pushing). Given the current environment, we do not think that this is an appropriate time to engage physicians and nurses about the trial guidelines, or physicians in audit feedback related to the trial. Furthermore, two of our sites (one intervention site and one control site) have temporarily closed their labour and delivery units during this time.